

REMARKS

The Examiner's Office Action mailed February 8, 2005, which rejected all pending claims, has been reviewed. Reconsideration in view of the foregoing amendments and remarks is respectfully requested. Moreover, Applicants have reviewed the Office Action of February 8, 2005, and submit that the above Amendments and the following Remarks are responsive to all points raised therein. Applicants believe that currently pending claims 1, 2 and 7-12 are now in form for allowance.

Status of Claims

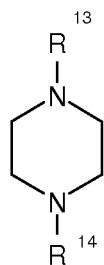
Claims 1, 2, and 7-12 are pending in the application. Claims 8 and 10 have been amended. New claims 11-12 have been added.

Claims 8 and 10 have been amended to correct orthographical errors. Support for new claims 11 and 12 can be found, for example, at pages 4, 12, 24, and 25 of the specification. No new matter has been added.

Rejection of Claim 1, 2, and 7-10 under 35 USC §102(b)

Reconsideration is respectfully requested of the rejection of claims 1, 2, and 7-10 under 35 U.S.C. §102(b) as being anticipated by Lee et al (WO 97/09331).

The claimed invention is directed to a method for increasing the endoparasitocidal action of cyclic depsipeptides. Independent claim 1 recites a method for increasing the endoparasitocidal action of cyclic depsipeptides by contacting endoparasites with cyclic depsipeptides in combination with piperazines. Independent claim 2 recites an endoparasitocidal composition that contains piperazines together with cyclic depsipeptides. The depsipeptides consist of amino acids and hydroxycarboxylic acids as ring units and having 24 ring atoms. New claims 11 and 12 narrow claim 2 by requiring the piperazines to correspond to the formula

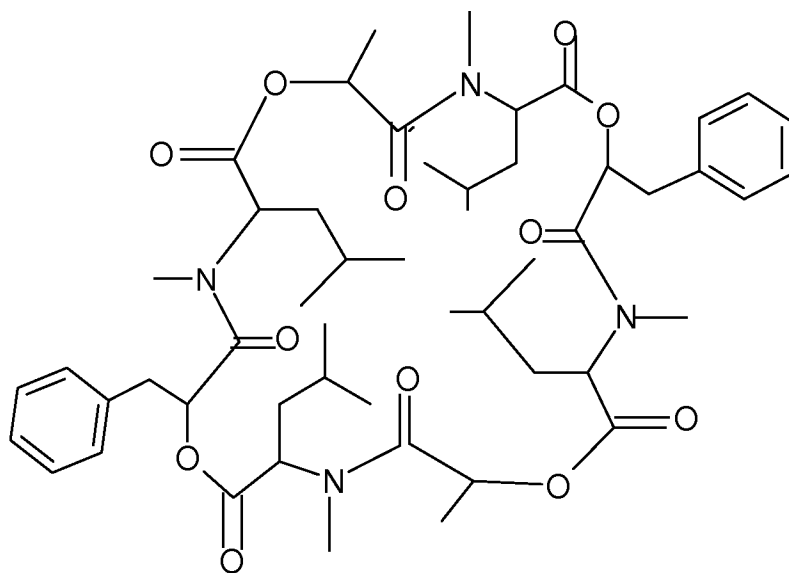


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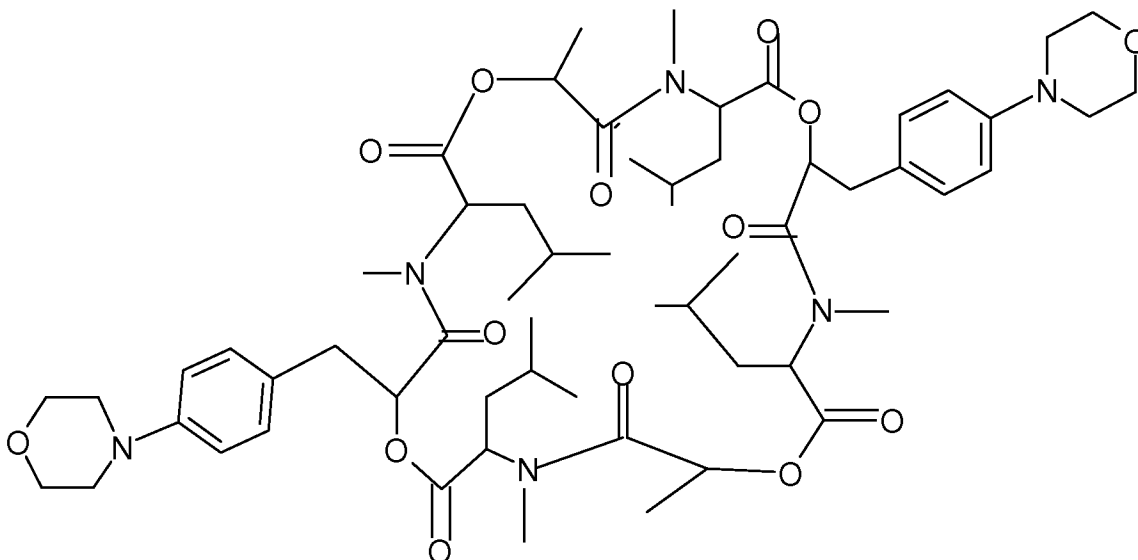
in which

R¹³ and R¹⁴ independently of one another represent identical or different substituents of the group hydrogen, in each case optionally substituted alkyl, cycloalkyl, aryl, heteroaryl, and –CON R¹⁵ R¹⁶ or –CSN R¹⁵ R¹⁶, in which R¹⁵ and R¹⁶ independently of one another represent identical or different substituents of the group hydrogen, in each case optionally substituted alkyl or cycloalkyl

And the cyclic dipeptides to correspond to the formula



for claim 11 and



for claim 12. As can be seen from the Applicants' biological examples, at page 25 of the specification, the combination of cyclic depsipeptides and piperazines is a mixture of an effective amount of cyclic depsipeptides and an effective amount of piperazines. The cyclic depsipeptides and piperazines are not chemically linked to each other.

To anticipate a claim, a reference must teach or suggest every element of the claim. Applicant respectfully submits that Lee et al. fail to teach or suggest every element of independent claims 1 and 2. In particular, Lee et al. fail to teach or suggest a method for increasing endoparasitocidal action of cyclic depsipeptides or an endoparasitocidal composition that includes cyclic depsipeptides consisting of amino acids and hydroxycarboxylic acids as ring units and having 24 ring atoms in combination with piperazines.

Lee et al. fail to teach a combination or mixture of cyclic depsipeptides and piperazines. Rather, as the Examiner acknowledges, Lee et al. teach a cyclic depsipeptide that incorporates a piperazine ring as a substituent or as integral part of the molecule. Lee et al. teach a structurally different compound than the claimed invention.

For all the reasons stated above, Lee et al. fail to teach each and every element of claims 1, 2, 11 and 12. Claims 7-10 each depend directly or indirectly from claims 1 and 2, and as such are patentable over Lee et al.

Rejection of Claims 1, 2, and 7-10 under 35 USC § 103(a)

Reconsideration is requested of the rejection of claims 1, 2, and 7-10 under §103(a) as being obvious in view of the combined teachings of Conder et al. 1995 (J. Antibiotics, 1995, 48/8:820-823) in view of Sangster et al. 1999 (Parasitology Today, April 1, 1999, 15/4:141-146).

Title 35 U.S.C. § 103(a) states that a patent shall not issue when “the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” The Supreme Court in *Graham v. John Deere* held that an obviousness determination is made by identifying: the scope and content of the prior art; the level of ordinary skill in the prior art; the differences between the claimed invention and prior art references; and secondary considerations. *Graham v. John Deere Co.*, 383 U.S. 1 (1966). To support a finding of obviousness, the initial burden is on the Office to apply the framework outlined in *Graham* and to provide some reason, suggestion, or motivation found either in the prior art references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the prior art reference or to combine prior art reference teachings to produce the claimed invention. *See Application of Bergel*, 292 F.2d 955, 956–57 (Fed. Cir. 1961).

Recently, the Supreme Court emphasized that the standard for obviousness is not rigid and should not be applied as such. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007). Instead, if the common sense of those skilled in the art could demonstrate why some combinations would have been obvious where others would not, then a claim can be found obvious even without an explicit teaching, suggestion, or motivation. As the Court stated in *KSR*, “it will be necessary for [the Office] to look at interrelated teachings of multiple [prior art references]; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by [one of] ordinary skill in the art, all in order to determine whether there was an

apparent reason to combine the known elements in the fashion claimed by the [patent application].” *Id.* at 1740–41.

Conder et al. teach the use of a cyclodepsipeptide, PF1022A, as an anthelmintic. Sangster et al. teach the use of piperazines as an anthelmintic in the treatment of horses. However, neither reference teaches or suggests a composition that includes a combination or mixture of piperazines and cyclodepsipeptides. Sangster et al. do discuss the resistance to anthelmintics and the need to identify other drug compounds to treat parasitic infections and diseases. The Examiner suggests that because of this discussion it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to combine two anthelmintics, specifically the two in the claimed invention, in an effort to create compositions that have improved endoparasiticial activity.

Applicants respectfully disagree. First, Sangster et al. focus on anthelmintic resistance and tools available for such research. It does not provide suggestions to one skilled in the art as to what may work as an anthelmintic or that a combination of anthelmintics would be successful at improving endoparasiticial activity. Second, according to Sangster et al. horses have been shown to have a resistance to piperazine. As such, the reference would seem to teach away from using piperazine as an anthelmintic rather than combining it with any other anthelmintic, as in the claimed invention. Finally, as shown in the Biological examples, at page 25 of the specification, one skilled in the art would consider the claimed invention unexpected or to have an unappreciated advantage. See *United States v. Adams*, 383 U.S. 39, 51-52 (1966) (indicating that a greater than expected result is an evidentiary factor relevant to nonobviousness). Although piperazines and cyclic depsipeptides, individually, were known to control endoparasiticial activity, the combination and improved results shown on page 25 of the specification are an unexpected advantage in view of the prior art.

For all the reasons stated above, Conder et al. in combination with Sangster et al. do not render claims 1, 2, 11 and 12 obvious. Claims 7-10 each

depend directly or indirectly from claims 1 and 2, and as such are patentable over Conder et al. and Sangster et al.

Conclusion

In view of the above, Applicants respectfully submit that the pending claims are novel and not obvious over the cited references and request withdrawal of all rejections and allowance of the claims.

The Commissioner is hereby authorized to charge any fee deficiency or credit any overpayment in connection with this amendment to Deposit Account No. 50-4260.

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